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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/066,513	01/30/2002	Judy Senior Pinsker	MAXIM.079C1	3651

20995 7590 12/03/2002

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EXAMINER
YOUNG, MICAH PAUL

ART UNIT	PAPER NUMBER
1615	6

DATE MAILED: 12/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/066,513	Applicant(s) PINSKER, JUDY SENIOR	
	Examin r Micah-Paul Young	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-17 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-17 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Acknowledgement of Papers Received: Information Disclosure Statement received 06/28/02

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

2. Claims 1, 3 – 5, and 9 – 14 are rejected under 35 U.S.C. 102(a) as being anticipated by Gehlsen (WO 00/40240). The claims are drawn to a transmucosal delivery formulation comprising histamine compositions. The formulation further comprises active agents, which can readily be absorbed through the mucosa, solvents, gelling agents, and absorption enhancers. Claims 12 – 14 are drawn to a method of administering the formulation comprising contacting the formulation with a mucosal membrane.

3. Gehlsen discloses a transmucosal formulation comprising histamine compounds. The formulation further comprises active agents, including vitamins and antibiotics, solvents including ethanol and water, absorption enhancers including fatty acid, and gelling agents cellulose derivatives (pg. 3, lin. 1 – 12; pg, 7, lin. 6 – 27; pg. 8, lin. 26 – 33; pg. 9, lin. 10 – 30; pg. 10, lin. 13 – 33; pg. 12, lin. 26 – 33). The formulation is applied to various sites on patients including oral mucosa sites (Examples). These disclosures render the claims anticipated.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. Claims 1 – 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gehlsen (WO 00/40240) in view of knowledge on the art. The claims are drawn to a transmucosal delivery formulation comprising histamine compositions. The formulation further comprises active agents, which can readily be absorbed through the mucosa, solvents, gelling agents, and absorption enhancers. Claims 2, 6 – 8 recite specific concentration of the components in the formulation. Claims 15 – 17 are drawn to a method of manufacturing a pharmaceutical composition where the permeation enhancer is a histamine compound. The composition further comprises an absorption enhancer.

As discussed above Gehlsen discloses essential elements of the claimed invention. The reference however does not disclose all of the concentrations claimed by applicant. The reference

presents the general transmucosal formulation comprising histamine compositions, active agents, solvents, gelling agents, and absorption enhancers. It has been held that where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *See* In re Aller, 220 F.2d 454 105 USPQ 233, 235 (CCPA 1955).

Furthermore the claims differ from the reference by reciting various concentrations of the active ingredients. However, the preparation of various transmucosal compositions having various amounts of the active is within the level of skill of one having ordinary skill in the art at the time of the invention. It has also been held that the mere selection of proportions and ranges is not patentable absent a showing of criticality. *See* In re Russell, 439 F.2d 1228 169 USPQ 426 (CCPA 1971).

7. Though the reference does not disclose the histamine compounds of its preparation to be permeation enhancers, the histamine compounds are present in the composition and perform their inherent duties. Histamines as well known in the art and defined by Encyclopedia Britannica, are vasodilators of blood vessels, (capillaries and arterioles) and critical in the inflammation response of the body, increasing the blood flow to an site of application ("histamine" *Encyclopedia Britannica* **http://www.seacrh.eb.com/eb/article?eu=41467**). When applied to the body, they dilate the blood vessels at the application situs causing an increase in blood flow. The increase in blood flow at the application situs would better the chances of the active substance to become absorbed by the body. This is an inherent property of histamine compounds, and does not impart patentability on the claimed invention. It would be

obvious to a skilled artisan that an increase in blood flow to an application situs would increase the chances of active substances being absorbed by the body.

8. With this in mind one of ordinary skill in the art would be motivated to modify the formulation of Gehlsen in order to optimize to effectiveness of the formulation at delivering the active agents. A skilled artisan would expect an increase in blood flow to the application situs of the patient in need thereof, and would expect an increase in active agent uptake into the blood stream due to the increase volume of blood. It would be obvious to a skilled artisan, at the time of the invention, to modify the teachings of Gehlsen with an expected result of a transmucosal delivery formulation comprising histamine compositions.

Conclusion

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Ecanow (USPN 4,963,367) discloses a transmucosal preparation comprising histamine compounds, solvents, other active agents and essential elements of the claimed invention. McMichael (USPN 4,521,405) discloses a preparation comprising histamine and a vaccine. Bechgaard et al (USPN 5,397,771) discloses a transmucosal preparation comprising histamine and other essential elements of the claimed invention.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Micah-Paul Young whose telephone number is 703-308-7005. The examiner can normally be reached on M-F 7:30am-4: 30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-746-7648 for regular communications and 703-746-7648 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1234.

Micah-Paul Young
Examiner
Art Unit 1615

M. Young
November 30, 2002

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600